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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/574,626	05/19/2000	Jose Remacle	VANM159.001AUS	7665

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EXAMINER	
ZHOU, SHUBO	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/574,626	Applicant(s) REMACLE ET AL.	
	Examiner Shubo (Joe) Zhou	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/22/03, 10/14/03, and 1/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

RCE

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/10/06, i.e. the IDS documents, has been received and considered.

Priority

2. It is noted that the RCE paper filed 1/10/06 indicates that certified foreign priority documents were filed. However, the copies of EP99870106.4 and EP00870025.4 filed 1/10/06 are not certified copies.

Applicants are reminded that MPEP section 201.14 states that "Unless provided in an application data sheet, 37 CFR 1.63 requires that the oath or declaration must identify the foreign application for patent or inventor's certificate for which priority is claimed under 37 CFR 1.55, and any foreign applications having a filing date before that of the application on which priority is claimed, by specifying the application number, country, day, month, and year of its filing. In the instant case, the declaration filed 9/25/2000 does not recognize these two prior foreign applications.

Information Disclosure Statement

3. The Information Disclosure Statements filed 5/22/03, 10/14/03 and 1/10/06 have been entered. Certain references listed on the PTO-1449 filed 1/10/06 have not been considered because no publication dates therefor have been provided. Initialed copies of the forms PTO-1449 are enclosed with this action.

Specification

4. The specification is objected to because of the following:

It appears that the phrase "Because if its metal nature, ..." recited on page 10, line 21, should be "Because of its metal nature, ..."

Appropriate correction is required.

Claim Rejections-35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 3-6, 9-10, 28 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (US patent No. 6,344,316, Issued Feb. 5, 2002, Filed June 25, 1997) in view of Hacker et al. (IDS document: Immunogold-silver staining -- autometallography : recent developments and protocols, In "Analytical Morphology: Theory, Applications & Protocols," Eds. Jiang Gu, Eaton Publishing, Chapter 2, pages 41-54, 1997).

The claims are drawn to a method of using a high density nucleic acid array for identifying and quantifying a target nucleic acid in a biological sample.

Lockhart et al. disclose a method for detecting nucleic acids using oligonucleotide array. The method comprises putting into contact target nucleic acids with capture molecules, i.e. oligonucleotides, which are fixed upon a surface of solid support according to an array with a density of more than about 60 different oligonucleotides per cm2. See columns 2 and 5. The method also comprises labeling the targets with different means including colorimetric labels such as colloidal gold. The binding of the oligonucleotides with targets leads to formation of precipitate. See column 24.

Lockhart et al., however, do not disclose performing a catalytic reduction of a metal present in solution leading to formation of a metallic precipitate in one or more regions.

Hacker et al. disclose a method of using immunogold-silver staining (IGSS) for the detection of nucleic acids and/or proteins. The method comprises hybridizing the nucleic acid samples on slides with nonradioactive methods such as biotin-labeled probes and detecting the hybridization using gold-labeled anti-biotin antibodies with subsequent autometallography (AMG). See page 47. The AMG is done with a solution comprising silver salt (i.e. silver ion donor) and a reducing agent such as hydroquinone where silver precipitate is formed in the regions where the gold is and where nucleic acids or proteins are. See page 42 and pages 49-50. Hacker et al disclose that "crystals of gold and silver and crystals where the lattices contain both a heavy metal (Ag, Au, Zn, Hg, Cu) and sulfide or selenide ions can be amplified." See page 42. Thus, the precipitate in the place where hybridization occurs actually comprises gold, silver or other metals as listed above. Some of these metals are magnetic. Hacker et al. further disclose that the presence of the precipitate is detected by microscopy. See page 41, Summary.

Hacker et al. state that AMG is highly specific and extremely sensitive and it allows silver amplification of catalytic crystals smaller than 0.5 nm. See page 42.

It would have been obvious at the time of the invention that one having ordinary skill in the art would have been motivated by Hacker et al. to modify the method of Lockhart et al. to adopt the AMG method for detection of nucleic acids in a sample using microarray to take AMG's advantage of being highly specific and extremely sensitive.

7. Claims 7-8, 11-27, 29, and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. and Hacker et al., as applied to claims 1, 4-6, 9, 28 and 33 above, in view of Abouzied et al. (Journal of AOAC International, Vol. 77, No. 2 (MAR-APR), pp. 495-501, 1994).

The claims are drawn to a method and an apparatus for using a high density array for identifying and quantifying a target compound in a biological sample involving forming a metallic precipitate at the position of the biomolecules on the array, wherein the binding between the capture molecule on the array and the target compounds is a reaction between an antigen and an antibody or a receptor and its ligand and wherein the detection of the presence of the precipitate and hence the biomolecules involves using an apparatus comprising CCD camera, etc.

As applied to claims 1, 4-6, 9, 28 and 33 above, the combination of Lockhart et al. and Hacker et al. discloses a method for detecting nucleic acids using oligonucleotide array.

However, Lockhart et al. and Hacker et al. do not disclose performing a catalytic reduction of a metal present in solution leading to formation of a metallic precipitate in one or more regions, do not show in their method that the binding between the capture molecule on the array and the target compounds in the sample is a reaction between an antigen and an antibody or a receptor and its ligand, and do not disclose an apparatus comprising a camera such as CCD.

Abouzied et al. disclose a method of simultaneously screening and detection of multianalyte using membrane strips. The method comprises the steps of contacting analytes (interpreted as the target compounds in the instant claims) with multiple antibodies (interpreted as the capture molecules of the instant claims) to let them bind; precipitation being formed on the membrane upon binding; detection and quantification of the precipitates by light reflection and video image analysis. The binding as disclosed is a reaction between an antigenic structure and its corresponding antibody as is required in the instant claims and the antibody and its corresponding antigen can be interpreted at a broad sense, as a receptor and its corresponding ligand, as required of the instant claims. The presence of the precipitates is detected by both visual detection of the color intensity by reflection, as required in the instant claims, and for quantification, image is taken by a CCD video camera and is converted into digital form (abstract and Experimental, pages 495-497). Abouzied et al. also disclose an apparatus, termed "a computer-assisted multianalyte assay system", for the detection and/or quantification of multianalytes, which apparatus comprises detection and/or quantification device including camera, and a computer to collect results including the images taken by the camera, as required in the instant claims (Figure 1 and page 497). A video-digitizing board is equipped with the CCD camera and is interpreted as the sensor as required in the instant claims. A computer program for performing the above steps is stored on a computer readable medium, which is in the broad sense the printed paper copy of the publication.

It would have been obvious at the time of the invention that since Lockhart et al. provide high density array and state that the method is rapid and simple to apply, and since Abouzied et al. provide methods for detecting not just nucleic acids, but also other molecules like

proteins/antigens, antibodies, or receptor-ligands using an array, a person having ordinary skill in the art would have been motivated by Abouzied et al. to modify the methods of Lockhart et al. and Hacker et al. to use the microarray technology for detection of, not only nucleic acids, but also proteins/antibodies and/or receptors/ligands to take the advantage of microarray's universal utilities in detecting multianalytes as disclosed by Abouzied et al.

8. Claims 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. and Hacker et al. in view of Abouzied et al., as applied to claims 1, 3-28, and 31-33 above, and further in view of Gingeras et al. (US patent # 6,228,575, issued May 8, 2001, filed Feb.7, 1997).

The claims are drawn to a method and an apparatus for using a high density array for identifying and quantifying a target compound in a biological sample involving forming a metallic precipitate at the position of the biomolecules on the array, wherein the detection of the presence of the precipitate and hence the biomolecules involves using an apparatus comprising CCD camera and bar code reader.

As applied to claims 1, 3-28, and 31-33 above, the combination of Lockhart et al., Hacker et al. and Abouzied et al. discloses such a method except using bar code and a bar code reader.

Gingeras et al. disclose a chip-based species identification using bar code and an apparatus comprising a computer system and bar code reader. Gingeras et al. disclose that the hybridization pattern of a particular sample is represented as a bar code in which the individual lines of the code indicates the presence of a certain pattern such as polymorphism. (see column 11 and Figures 14, 15, and 32).

Given that bar code and bar code readers would have been used in various applications including that disclosed by Gingeras et al., it would have been obvious at the time of the invention that one having ordinary skill in the art would have been motivated by Gingeras et al.

to modify the method as disclosed in combination by Lockhart et al., Hacker et al. and Abouzied et al. to use the simple method of bar code and bar code reader to take advantage of its convenience and speed.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shubo (Joe) Zhou, Ph.D.

Patent Examiner

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER